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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/067,451	02/05/2002	Ronald Brown Miller	222.1101CON	8520

23280 7590 10/18/2002

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1615	8

DATE MAILED: 10/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,451	MILLER ET AL.	
	Examiner	Art Unit	
	Lakshmi S Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 11-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 11-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Receipt of response to election requirement and amendment B, dated 7-22-02 is acknowledged.

Election/Restrictions

1. Applicant's election without traverse of Group I in Paper No. 6 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-5, 8 and 11, 12, 15-17, 22-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Instant independent claims 1 and 11 recite a solid, oral, controlled release pharmaceutical dosage form comprising a pharmaceutically active ingredient having solubility in water of greater than 1gm in 250ml water, and the said active ingredient is dispersed in a matrix. Independent claim 1 further recites a specific dissolution rate as tested by Ph. Eur. Basket method and a specific Tmax and a specific ratio of Cmax to mean plasma level. However, the limitation "pharmaceutically active ingredient having a solubility in water of greater than 1gm in 250ml water", is very broad and includes any water soluble active ingredient that is known to-date and even extends to any ingredient that would be discovered in future. Instant disclosure

only mentions hydromorphone hydrochloride, diamorphone hydrochloride, tramadol hydrochloride and dihydrocodeine tartarate, as water-soluble drugs that are suitable for the instant formulation. There is an insufficient written descriptive support for the generic limitation as it includes any undisclosed active agents that fall under the above category.

The dependent claims are also being rejected, as they are dependent upon the independent claim for this limitation.

3. Claims 1-5, 8 and 11, 12, 15-17, 22-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a solid, oral, controlled release dosage form comprising a pharmaceutically active ingredient having solubility in water of greater than 1gm in 250ml water, and the said active ingredient is dispersed in a matrix, which provides the claimed release rate as tested by Ph. Eur. Basket method at 100 rpm and 900ml aqueous buffer (pH 6.5) containing 0.05% w/w Polysorbate 80 at 37 degrees C, does not reasonably provide enablement for achieving the claimed zero order relelase rate & specific release parameters using the same method with any type of matrix in which an active ingredient is dispersed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Instant claims are directed to oral, solid, controlled release formulations that exhibit a specific release pattern, when tested using a specific method. The claims encompass any water-soluble active agent and any matrix material for dispersing the active agent, to achieve the release rate. Oral, controlled release dosage formulations for water-soluble and water insoluble active agents are very well known in the art (A copy of the Remington: The science and practice of Pharmacy is attached, which shows the state of the art on controlled release dosage forms pages 1660-1668). Sustained release formulations (include controlled as well as prolonged release forms) in general achieve a slow release of drug over an extended period of time, which depends on a number of factors such as solubility and pKa of the drug, drug stability, absorption of the drug, elimination and biological half life of the drug, side effects and safety concentrations, type of matrix material used etc. A number of matrix materials, generally categorized as insoluble plastic materials (methacrylate, polyvinyl chloride or polyethylene), hydrophilic polymers (such as methylcellulose, hydroxypropylmethylcellulose etc) and fatty compounds (waxes or fatty acid esters), are used to disperse the active agents. Thus, employing

the same matrix material, one of an ordinary skill in the art would be able to achieve different release rates for a given active agent, depending on the properties of the active agent. Further, the in vitro dissolution of the active agent dispersed in the matrix is measured using standard pharmacological methods such as Ph. Eur. Basket Method, Ph. Eur. Paddle Method etc., using different buffers, and experimental conditions such as pH, temperature etc. The in vitro dissolution rate of an active agent is correlated to its in vivo bioavailability. However, the in vitro dissolution rate does not always yield the same absorption parameters such as Cmax, Tmax because the latter depends on the dosage administered and absorption half-life of the active agent.

Thus, a sustained or controlled release formulation containing a water-soluble drug dispersed in a matrix may yield a different dissolution rate depending upon the test method employed. In this regard, instant specification only describes the release rates of one specific drug, using a matrix made of a hydrophilic polymer and a hydrophobic material. The specification does not provide any guidance to one of an ordinary skill in the art to extrapolate the release rate achieved for a drug using one particular method to any matrix polymer and any drug. Given the knowledge, as described above, that the relelase rate is a function of several rate limiting steps, one of ordinary skill in the art would not know how any active agent, dispersed in any kind of matrix results in the same relelase rate (as claimed). From the teachings standard in the art, one of an ordinary skill in the art would not be able to find a correlation between the matrix polymer used and the specific test method used to specifically achieve the claimed release rate. Accordingly, absent any guidance one of an ordinary skill in the art would have to perform undue experimentation so to optimize the combination of each and every active agent with every

suitable matrix polymer that yields the claimed in vitro dissolution rate, when tested by the claimed method. Furthermore, absent any descriptive guidance a skilled artisan would not be able to achieve the same plasma concentrations, Tmax and Cmax values, as claimed, using any active agent, any matrix material and the specific method.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 17 recites the limitation "the weight ratio of hydrophobic fusible material to hydrophilic organic polymeric wicking agent" in lines 1-3. There is insufficient antecedent basis for this limitation in the claim.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims(s) because the examined claim is either anticipated by, or would have been obvious over the reference claims(s). See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-8 and 11-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 and 11-22 of U.S. Patent No. 6,399,096. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant solid, oral, controlled relelase formulations are generic to all water-soluble active ingredients, including the,specific drugs such as morphine, tramadol etc., of the patented claims. Besides, both sets of claims recite that the drug is dispersed in a matrix, which results in the same in vitro dissolution rates. Accordingly, the species of the patented claims anticipates the claimed genus of the instant application, and therefore, a patent to the genus would necessarily, extend the rights of the species should the genus issue as a patent after the species.

6. Claims 1-8 and 11-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-33 of U.S. Patent No. 5,965,163. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant solid, oral, controlled relelase formulations are generic to the particulate solid dosage forms of the patented claims because instant dependent claim recite microparticulates. Besides, both sets of claims recite the similar of matrix and also morphine as the active agent in the dependent claims. Instant claim 11 recites the product by process claim, which overlaps with the patented product by process claims. Absent any distinction in the active agent or matrix materials, the patented solid dosage form inherently possess the ability to produce the claimed release rates, as tested by the specified method of instant claims. Accordingly, the species of the patented claims anticipates the claimed genus of the instant application, and therefore, a patent to

the genus would necessarily, extend the rights of the species should the genus issue as a patent after the species.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-4, 8, 11, 12, 14-17 and 23-25 are rejected under 35 U.S.C. 102(b) as being anticipated by US 4,828,836 to Elger et al (hereafter Elger).

Instant claim 1 is directed to an oral, a solid, controlled release pharmaceutical formulation comprising an active agent and a matrix in the formulation. Claim 1 recites specific solubility of the active agents and recites specific relelase patterns of the active agent, as tested by Ph. Eur. Basket Method. Claim 1 primarily requires two components an active agent and a matrix. Dependent claim 4 recites that the matrix comprises a mixture of hydrophobic fusible material having a melting point of greater than 40 degrees C and a hydrophilic polymeric fusible wicking agent. Claim 8 recites a solid controlled release formulation prepared by the recited process steps.

Elger discloses a solid, controlled release pharmaceutical formulation comprising an active agent incorporated in a controlled release matrix comprising a water-soluble polydextrose, for achieving a slow relelase of drug over extended periods of time. (Col. 1). Elger discloses that the matrix also contains at least one digestible C8-C50 substituted or unsubstituted hydrocarbon, especially a C12-C36 fatty alcohol such as polyethylene glycol and optionally contains

hydroxyalkyl or carboxyalkylcellulose (col. 2, lines 11-35). The matrix polymer, polydextrose, and polyethylene glycol taught by Elger read on the instant matrix materials. Although Elger does not state the melting point as claimed, the property is inherent to the compounds because instant specification also states polyethylene glycol as the suitable hydrophobic agent having the claimed melting point. Elger also discloses tablets and capsule, as claimed. The teachings of pellets and granules by Elger meet the claimed particulates because the instant claims do not state the particle size. With respect to the limitations regarding specific release rates, dissolution parameters i.e., ratio of Cmax to mean plasma levels, tmax, W50 etc., and the claimed test method, it is examiner's position that because Elger discloses claimed polymers of the matrix and also discloses various active agents (col. 3) that include the water soluble active agents (for example theophylline in col. 8 and pyridoxine hydrochloride in col. 8, both of which are water soluble), the release rates claimed are inherent to the compositions. Applicant's attention is also directed to the enablement rejection under 35 USC 112, first paragraph (above). Elger further discloses that the release of the active agent is achieved for a long time i.e., 8 hours or more (col. 1, lines 7-12) and figure 2 shows that the release is achieved over 15 –20 hours. With respect to claim 11, the limitation "the dosage form being obtainable by a process comprising:" is an intended use and the process is not a positive limitation. Furthermore, even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elger et al (hereafter Elger).

Instant claims recite a specific ratio of hydrophobic fusible agent and the polymer.

Elger, discussed above, fails to teach exactly the same ratios as claimed, 8:1 to 16:1 and instead teaches a ratio of 1:4 to 4:1. However, the examples of solid controlled relelase compositions taught by Elger (in cols. 7 and 8), Elger teaches a higher amount of hydrophobic polyethylene glycol as compared to polydextrose. Further, Elger teaches the above matrix components for the same purpose as claimed. Accordingly, optimizing the amounts of the hydrophobic and hydrophilic agents in the compositions of Elger so as to achieve a sustained release rate of a given active agent would have been obvious for one of an ordinary skill in the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S Channavajjala whose telephone number is 703-308-2438. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-7924 for regular communications and 703-308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Lakshmi S Channavajjala
Examiner
Art Unit 1615

October 15, 2002

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600